IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Application of: DANILO PORRO MICHAEL SAUER Serial No.: 10/606,300 Filed: June 25, 2003 For: ASCORBIC ACID PRODUCTION FROM YEAST	Confirmation No.: 8974 Group Art Unit: 1636 Examiner: Walter Schlapkohl Attorney Docket: 2027.594097/RFE 2005942 **CUSTOMER NO. 23720**

REPLY BRIEF

Commissioner for Patents
P. O. Box 1450
Alexandria, VA 22313-1450

Sir:

Applicants hereby submit a Reply Brief. No fee should be required for filing this Reply Brief. If any fee is required, the Director is authorized to deduct the fee from Williams, Morgan & Amerson, P.C. Deposit Account No. 50-0786/2027.594097RE.

I. The Appeal Brief Contains All Information Required by 37 C.F.R. § 1.192(c)

Applicants agree with the Examiner's statements regarding the real party in interest and related appeals, interferences, or judicial proceedings at sections 1 and 2 of the Examiner's Answer dated June 19, 2007 ("the Answer"). Applicants acknowledge that the Examiner has found their statements regarding the status of claims, the status of amendments after final rejection, the summary of claimed subject matter, the grounds of rejection to be reviewed on appeal, and the claims appendix at sections 3-7 of the Answer to be correct.

II. Applicants' Reply to Examiner's Statement of Grounds of Rejection

A. Rejection of claims 12-14 under 35 U.S.C. § 112, first paragraph, as failing to comply with the written description requirement

Claims 12-14 are directed to methods of generating ascorbic acid comprising obtaining a recombinant yeast capable of converting an ascorbic acid precursor into ascorbic acid, wherein the yeast is functionally transformed with a coding region either encoding L-galactose dehydrogenase (LGDH) enzyme having at least about 90% similarity with SEQ ID NO:11 or at least about 90% identity with SEQ ID NO:11, or having at least about 90% identity with SEQ ID NO:12. Applicants thank the Examiner for pointing out the unintentionally erroneous categorization of LGDH as L-galactono-1,4-lactone dehydrogenase made at p. 5, line 12 to p. 6, line 1 of the Appeal Brief. As the Examiner understood in the Answer, LGDH refers to L-galactose dehydrogenase, which catalyzes the conversion of L-galactose to L-galactono-1,4-lactone.

Applicants also wish to correct a mischaracterization of the claims made by the Examiner at a number of places in the Answer, *e.g.*, p. 14, lines 5-10. The Examiner wrote that the person

of ordinary skill in the art could not be guided to "a variant with 90% similarity or 90% identity to SEQ ID NO:11 *capable of converting any precursor into ascorbic acid upon transformation into yeast*" (emphasis in original). The claims do *not* recite an *LGDH* having at least about 90% similarity or at least about 90% identity to SEQ ID NO:11 capable of converting any precursor into ascorbic acid; instead, the claims plainly recite the use of a yeast that *both* (i) is capable of converting an ascorbic acid precursor into ascorbic acid *and* (ii) is functionally transformed with a coding region encoding an LGDH having a recited structural property. It is the *yeast* that is claimed to perform the conversion, *not* the coding region encoding the LGDH with which the yeast is functionally transformed. Whether the LGDH enzyme in the yeast catalyzes the conversion of the precursor to ascorbic acid is not relevant; the claims encompass both yeast in which the LGDH enzyme catalyzes the conversion of the precursor to ascorbic acid and yeast in which it does not.

The question on which Applicants' appeal hinges is whether the two exemplary strains of yeast functionally transformed with a coding region encoding an LGDH, specifically in both yeast strains, a coding region encoding an LGDH having the sequence of SEQ ID NO:11 and having identity with the native LGDH of *Arabidopsis thaliana*, disclosed in the application provide written description for a method of using any one of a genus of recombinant yeast functionally transformed with a coding region either encoding an LGDH having at least about 90% similarity with SEQ ID NO:11, at least about 90% identity with SEQ ID NO:11, or having at least about 90% identity with SEQ ID NO:12.

Applicants submit they have satisfied the written description requirement for the genus of recombinant yeast recited by the present claims by disclosing relevant, identifying characteristics sufficient to show they were in possession of the claimed genus. Specifically, Applicants have

shown a functional characteristic, namely, the ability to catalyze conversion of L-galactose to L-galactono-1,4-lactone (which renders an enzyme an "LGDH"), coupled with a correlation between function and structure, namely, the correlation between LGDH activity and an enzyme having the sequence of SEQ ID NO:11.

The Examiner has repeatedly turned to *Regents of the University of California v. Eli Lilly*, 119 F.3d 1559, 43 USPQ2d 1398 (Fed. Cir. 1997) to support his contention that the present claims fail to comply with the written description requirement. *Lilly* is not applicable to the facts of the present case. The *Lilly* court held that the disclosure of a rat-insulin encoding cDNA did not provide sufficient written description for the genera of "mammalian insulin cDNA" or "vertebrate insulin cDNA." These facts are distinct over the facts of the present case in a number of ways. First, as is known to a person of ordinary skill in the art, a cDNA is a nucleic acid molecule derived from (actual or conceptual) reverse transcription of an mRNA molecule encoding a particular protein. The term "cDNA" therefore requires knowledge or discovery of the sequence of the mRNA molecule encoding the particular protein. Given the degeneracy of the genetic code, many possible mRNA sequences could encode a particular protein sequence, and therefore the sequence of a cDNA can only be determined or predicted after possession of its corresponding mRNA sequence. For these reasons, the *Lilly* court held that a description of the amino acid sequence of human insulin did not provide written description of the cDNA sequence encoding human insulin, because an amino acid sequence cannot be used to derive a cDNA sequence. In contrast, in the present application, the term "LGDH" refers to an enzyme having a particular function (*i.e.*, catalysis of the conversion of L-galactose to L-galactono-1,4-lactone) and is independent of any actual or conceptual derivation of that function from a particular protein or nucleic acid molecule.

Second, the *Lilly* court held that the genera of "mammalian insulin cDNA" or "vertebrate insulin cDNA" were distinguished from other genera solely on functional terms (43 USPQ2d at 1406). The genus recited by claims 12-14 distinguishes over other genera by *both* the LGDH function *and* structural features commonly possessed by members of the genus that distinguish them over others (*i.e.*, the limitations to particular sequences recited by the claims).

Even if *Lilly* could properly be applied to the facts of the present case, Applicants' view is supported by it and other cases cited by the Examiner. The Examiner cites MPEP 2603, which cites *Lilly* and other cases, as holding "when there is substantial variation within the genus, one must describe a sufficient variety of species to reflect the variation within the genus." No substantial variation exists within the genus of LGDH enzymes having at least about 90% similarity with SEQ ID NO:11 or at least about 90% identity with SEQ ID NO:11, or coding regions having at least about 90% identity with SEQ ID NO:12. No substantial variation exists in the genus of enzymes able to catalyze conversion of L-galactose to L-galactono-1,4-lactone, *i.e.*, the genus of LGDHs. Any variation between enzymes of this genus would be in the realm of reaction kinetics, *e.g.*, how fast the conversion would take place or what the equilibrium levels of L-galactose and L-galactono-1,4-lactone in the absence of addition or removal of either or both compounds would be; such variation would not be "substantial." If no substantial variation exists within the genus of LGDHs, it follows that no substantial variation can exist within the narrower subgenus of LGDHs having at least about 90% similarity with SEQ ID NO:11 or at least about 90% identity with SEQ ID NO:11, or being encoded by coding regions having at least about 90% identity with SEQ ID NO:12. Further, no unpredictability exists in the results obtained from species other than those specifically enumerated. Any member of the genus of LGDHs would predictably have the ability to catalyze conversion of L-galactose to L-galactono-

1,4-lactone. Therefore, any member of the narrower subgenus recited by the present claims would predictably have this ability.

From the above discussion, it is clear that the person of ordinary skill in the art would have been able to envision a sufficient number of specific embodiments that meet the functional limitations of the claims to describe the claimed genus. Therefore, Applicants submit claims 12-14 comply with the written description requirement.

III. Conclusion

Applicants submit that all the pending rejections should be overruled and claims 12-14 should be allowed.

Respectfully submitted,

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July 12, 2007

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